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NEWS	4	AUG 24	ENCOMPLIT/ENCOMPLIT2 reloaded and enhanced
NEWS	5	AUG 24	CA/CAplus enhanced with legal status information for U.S. patents
NEWS	6	SEP 09	50 Millionth Unique Chemical Substance Recorded in CAS REGISTRY
NEWS	7	SEP 11	WPIDS, WPINDEX, and WPIX now include Japanese FTERM thesaurus
NEWS	8	OCT 21	Derwent World Patents Index Coverage of Indian and Taiwanese Content Expanded
NEWS	9	OCT 21	Derwent World Patents Index enhanced with human translated claims for Chinese Applications and Utility Models
NEWS	10	NOV 23	Addition of SCAN format to selected STN databases
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NEWS	12	DEC 01	FRFULL Content and Search Enhancements
NEWS	13	DEC 01	DGENE, USGENE, and PCTGEN: new percent identity feature for sorting BLAST answer sets
NEWS	14	DEC 02	Derwent World Patent Index: Japanese FI-TERM thesaurus added
NEWS	15	DEC 02	PCTGEN enhanced with patent family and legal status display data from INPADOCDB
NEWS	16	DEC 02	USGENE: Enhanced coverage of bibliographic and sequence information

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=> s SZKUDLINSKI M?/AU
L1         227 SZKUDLINSKI M?/AU

=> s l1 and (FSH or follicle(w)stimulating(w)hormone)
L2          22 L1 AND (FSH OR FOLLICLE(W) STIMULATING(W) HORMONE)

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3          10 DUP REM L2 (12 DUPLICATES REMOVED)

=> s WEINTRAUB B?/AU
L4        1178 WEINTRAUB B?/AU

=> s l4 and (FSH or follicle(w)stimulating(w)hormone)
L5          84 L4 AND (FSH OR FOLLICLE(W) STIMULATING(W) HORMONE)

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6          34 DUP REM L5 (50 DUPLICATES REMOVED)

=> dis ibib abs l3 1-10

L3   ANSWER 1 OF 10  BIOSIS  COPYRIGHT (c) 2009 The Thomson Corporation  on STN
ACCESSION NUMBER:   2006:650039  BIOSIS
DOCUMENT NUMBER:    PREV200600661389
TITLE:              Follicle stimulating hormone
                    superagonists.
AUTHOR(S):          Anonymous; Szkudlinski, Mariusz W. [Inventor];
                    Weintraub, Bruce D. [Inventor]; Grossmann, Mathis
                    [Inventor]
CORPORATE SOURCE:   Potomac, MD USA
                    ASSIGNEE: The United States of America as represented by
                    the Department of Health and Human Services
PATENT INFORMATION: US 07070788 20060704
SOURCE:             Official Gazette of the United States Patent and Trademark
                    Office Patents, (JUL 4 2006)
                    CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE:      Patent
LANGUAGE:           English
ENTRY DATE:         Entered STN: 29 Nov 2006
                    Last Updated on STN: 29 Nov 2006
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AB The invention is directed toward a human glycoprotein hormone having at least one, two, three, four, or five basic amino acids in the alpha-subunit at positions selected from the group consisting of positions 11, 13, 14, 16, 17, and 20. The inventions is also directed to a human glycoprotein where at least one of the amino acids at position 58, 63, and 69 of the beta-subunit of the human thyroid stimulating hormone are basic amino acids. The invention is further directed to a modified human glycoprotein hormone having increased activity over a wild-type human glycoprotein hormone, where the modified human glycoprotein comprises a basic amino acid substituted at a position corresponding to the same amino acid position in a non-human glycoprotein hormone having an increased activity over the wild-type human glycoprotein hormone. The invention is also directed to a method of constructing superactive nonchimeric analogs of human hormones comprising comparing the amino acid sequence of a more active homolog from another species to the human hormone, and selecting superactive analogs from the substituted human hormones. The invention is also directed to nucleic acids encoding the modified human glycoprotein hormones, vectors containing those nucleic acids, and host cells containing those vectors.

L3 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:1154787 CAPLUS
DOCUMENT NUMBER: 143:411096
TITLE: Human glycoprotein hormone superagonists and uses thereof
INVENTOR(S): Szkudlinski, Mariusz W.; Weintraub, Bruce D.
PATENT ASSIGNEE(S): Trophogen, Inc., USA
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005101000	A2	20051027	WO 2005-US8957	20050318
WO 2005101000	A3	20061123		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005233923	A1	20051027	AU 2005-233923	20050318
CA 2561545	A1	20051027	CA 2005-2561545	20050318
EP 1738174	A2	20070103	EP 2005-732628	20050318
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
CN 1965234	A	20070516	CN 2005-80017466	20050318
BR 2005009469	A	20070911	BR 2005-9469	20050318
JP 2007530974	T	20071101	JP 2007-506215	20050318
US 20090214424	A1	20090827	US 2006-594843	20060928
MX 2006011290	A	20070321	MX 2006-11290	20060929
IN 2006KN03161	A	20070608	IN 2006-KN3161	20061030
PRIORITY APPLN. INFO.:			US 2004-557704P P	20040331

WO 2005-US8957 W 20050318
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB The present invention provides improved methods of imaging, targeted therapy and detection and diagnostics using modified glycoprotein hormones having increased activity over wild-type hormones. The methods involve assaying for an analyte that interferes with the binding of a modified glycoprotein hormone to a glycoprotein hormone receptor. Targeted delivery of therapeutic agents coupled to a modified glycoprotein hormone is also claimed.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:1049828 CAPLUS
DOCUMENT NUMBER: 143:339960
TITLE: Follicle-stimulating hormone superagonists with improved potency, pharmacokinetics and plasma half-life
INVENTOR(S): Szkudlinski, Mariusz W.; Weintraub, Bruce D.
PATENT ASSIGNEE(S): Trophogen, Inc., USA
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005089445	A2	20050929	WO 2005-US8960	20050318
WO 2005089445	A3	20080221		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, AP, EA, EP, OA				
AU 2005223651	A1	20050929	AU 2005-223651	20050318
CA 2563345	A1	20050929	CA 2005-2563345	20050318
EP 1734979	A2	20061227	EP 2005-732601	20050318
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
US 20070219116	A1	20070920	US 2006-593466	20060919
MX 2006011898	A	20080613	MX 2006-11898	20061013
IN 2006KN03017	A	20070608	IN 2006-KN3017	20061018
CN 101189259	A	20080528	CN 2005-80015850	20061117

PRIORITY APPLN. INFO.: US 2004-554419P P 20040319
WO 2005-US8960 W 20050318
ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB This invention provides superactive analogs of FSH demonstrating enhanced bioactivity both in vitro and in vivo as compared to wild type FSH. In particular, the analogs of the invention demonstrate at least a 10-fold increase in potency or at least a 10% increase in maximal efficacy as compared to wild type protein. Preferred α-subunit mutations comprise at least two basic amino acids at positions corresponding to positions 13, 14, 16, 17, 20, 21,22, 66, 68, 73,74, and

81, and a modified β-subunit comprises at least one basic amino acid at a position corresponding to any one of positions 2,4,14,63,64, 67, and 69. Sequences providing potential glycosylation recognition sites may be either an N-terminal or C-terminal extension on either the α or β chain. One of the analogs of the invention (designated TR-4402) comprises the substitutions α(E14R+Q20R+Q20R) + β(E4R). The analogs are particularly useful for treating subjects showing low FSH receptor expression or poor FSH receptor responsiveness, and for the treatment of any condition associated with glycoprotein hormone activity.

L3 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:746157 CAPLUS
DOCUMENT NUMBER: 128:19051
ORIGINAL REFERENCE NO.: 128:3634h,3635a
TITLE: Glycoprotein hormone superagonists, their preparation with recombinant cells, and their use in treatment of diseases and dysfunctions
INVENTOR(S): Szkudlinski, Mariusz W.; Weintraub, Bruce D.; Grossman, Mathis
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA; Szkudlinski, Mariusz W.; Weintraub, Bruce D.; Grossman, Mathis
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9742322	A1	19971113	WO 1996-US6483	19960508
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2253441	A1	19971113	CA 1996-2253441	19960508
AU 9658549	A	19971126	AU 1996-58549	19960508
AU 714635	B2	20000106		
EP 954578	A1	19991110	EP 1996-920151	19960508
EP 954578	B1	20071219		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 2000509603	T	20000802	JP 1997-539866	19960508
JP 3981413	B2	20070926		
AT 381617	T	20080115	AT 1996-920151	19960508
EP 1947117	A2	20080723	EP 2007-150018	19960508
EP 1947117	A3	20081008		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US 6361992	B1	20020326	US 1998-185408	19981103
KR 2000010866	A	20000225	KR 1998-709010	19981107
US 20020110909	A1	20020815	US 2002-57113	20020125
US 7070788	B2	20060704		
US 20060183672	A1	20060817	US 2006-409428	20060421
JP 2007259860	A	20071011	JP 2007-124785	20070509
JP 4081130	B2	20080423		
JP 2008079619	A	20080410	JP 2007-317316	20071207
US 20090233846	A1	20090917	US 2009-467081	20090515
PRIORITY APPLN. INFO.:			EP 1996-920151 A3	19960508

JP 1997-539866	A3	19960508
WO 1996-US6483	A	19960508
US 1998-185408	A3	19981103
US 2002-57113	A1	20020125
US 2006-409428	A3	20060421
JP 2007-124785	A3	20070509

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention is directed toward a human glycoprotein hormone having at least one, two, three, four or five basic amino acids in the α-subunit at positions selected from the group consisting of positions 11, 13, 14, 16, 17 and 20. The invention is also directed to a human glycoprotein where at least one of the amino acids at positions 58, 63 and 69 of the β-subunit of the human TSH are basic amino acids. The invention is also directed to a method of constructing superactive nonchimeric analogs of human hormones comprising comparing the amino acid sequence of a more active homolog from another species to the human hormone, substituting selected amino acids in the human hormone with the corresponding amino acids from the other species, determining the activity of the substituted human hormones, and selecting superactive analogs from the substituted human hormones. The invention is also directed to nucleic acids encoding the modified human glycoprotein hormones, vectors containing those nucleic acids, and host cells containing those vectors. The superagonists may be used in treatment of diseases such as thyroid carcinoma and disfunctions such as infertility. Multiply substituted human TSH (i.e., A13K, P16K and Q20K in the α subunit and L69R in the β subunit) displayed a 95.7-fold increase in potency relative to wild-type TSH.

OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 10 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 1997407919 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9261143

TITLE: Human thyroid-stimulating hormone (hTSH) subunit gene fusion produces hTSH with increased stability and serum half-life and compensates for mutagenesis-induced defects in subunit association.

AUTHOR: Grossmann M; Wong R; Szkudlinski M W; Weintraub B D

CORPORATE SOURCE: Department of Medicine, University of Maryland School of Medicine and the Institute of Human Virology, Medical Biotechnology Center, Baltimore, Maryland 21201, USA.. grossman@umbi.umd.edu

SOURCE: The Journal of biological chemistry, (1997 Aug 22) Vol. 272, No. 34, pp. 21312-6.
Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199709

ENTRY DATE: Entered STN: 26 Sep 1997
Last Updated on STN: 26 Sep 1997
Entered Medline: 15 Sep 1997

AB The human thyroid-stimulating hormone (hTSH) subunits alpha and beta are transcribed from different genes and associate noncovalently to form the bioactive hTSH heterodimer. Dimerization is rate-limiting for hTSH secretion, and dissociation leads to hormone inactivation. Previous studies on human chorionic gonadotropin (hCG) and human follicle -stimulating hormone had shown that it was possible by

subunit gene fusion to produce a bioactive, single chain hormone. However, neither the stability nor the clearance from the circulation of such fused glycoprotein hormones has been studied. We show here that genetic fusion of the hTSH alpha- and beta-subunits using the carboxyl-terminal peptide of the hCG beta-subunit as a linker created unimolecular hTSH whose receptor binding and bioactivity were comparable to native hTSH. Interestingly, the fused hTSH had higher thermostability and a longer plasma half-life than either native or dimeric hTSH containing the hCG beta-subunit-carboxyl-terminal peptide, suggesting that dimer dissociation may contribute to glycoprotein hormone inactivation in vivo. In addition, we show for the first time that synthesis of hTSH as a single polypeptide chain could overcome certain mutagenesis-induced defects in hTSH secretion, therefore enabling functional studies of such mutants. Thus, in addition to prolongation of plasma half-life, genetic fusion of hTSH subunits should be particularly relevant for the engineering of novel analogs where desirable features are offset by decreased dimer formation or stability. Such methods provide a general approach to expand the spectrum of novel recombinant glycoprotein hormones available for in vitro and in vivo study.

L3 ANSWER 6 OF 10 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1997326138 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9182589
TITLE: Substitution of the seat-belt region of the thyroid-stimulating hormone (TSH) beta-subunit with the corresponding regions of choriogonadotropin or follitropin confers luteotropic but not follitropic activity to chimeric TSH.
AUTHOR: Grossmann M; Szkudlinski M W; Wong R; Dias J A; Ji T H; Weintraub B D
CORPORATE SOURCE: Laboratory of Molecular Endocrinology, Department of Medicine, University of Maryland School of Medicine and the Institute of Human Virology, Medical Biotechnology Center, Baltimore, Maryland 21201, USA.. grossman@umbi.umd.edu
SOURCE: The Journal of biological chemistry, (1997 Jun 13) Vol. 272, No. 24, pp. 15532-40.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 24 Jul 1997
Last Updated on STN: 24 Jul 1997
Entered Medline: 14 Jul 1997

AB The region between the 10th and 12th cysteine (Cys88-Cys105 in human thyroid-stimulating hormone beta-subunit (hTSHbeta)) of the glycoprotein hormone beta-subunits corresponds to the disulfide-linked seat-belt region. It wraps around the common alpha-subunit and has been implicated in regulating specificity between human choriogonadotropin (hCG) and human follicle-stimulating hormone (hFSH), but determinants of hTSH specificity are unknown. To characterize the role of this region for hTSH, we constructed hTSH chimeras in which the entire seat-belt region Cys88-Cys105 or individual intercysteine segments Cys88-Cys95 and Cys95-Cys105 were replaced with the corresponding sequences of hCG and hFSH or alanine cassettes. Alanine cassette mutagenesis of hTSH showed that the Cys95-Cys105 segment of the seat-belt was more important for TSH receptor binding and signal transduction than the Cys88-Cys95 determinant loop region. Replacing the entire seat-belt of hTSHbeta with the hCG sequence conferred full hCG receptor binding and activation to the hTSH chimera, whereas TSH receptor binding and activation were abolished. Conversely, introduction of the hTSHbeta

seat-belt sequence into hCGbeta generated an hCG chimera that bound to and activated the TSH receptor but not the CG/lutropin (LH) receptor. In contrast, an hTSH chimera bearing hFSH seat-belt residues did not possess any follitropic activity, and its thyrotropic activity was only slightly reduced. This may in part be due to the fact that the net charge of the seat-belt is similar in hTSH and hFSH but different from hCG. However, exchanging other regions of charge heterogeneity between hTSHbeta and hFSHbeta did not confer follitropic activity to hTSH. Thus, exchanging the seat-belt region between hTSH and hCG switches hormonal specificity in a mutually exclusive fashion. In contrast, the seat-belt appears not to discriminate between the TSH and the FSH receptors, indicating for the first time that domains outside the seat-belt region contribute to glycoprotein hormone specificity.

L3 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:340938 CAPLUS
DOCUMENT NUMBER: 125:26466
ORIGINAL REFERENCE NO.: 125:4999a,5002a
TITLE: Site-directed mutagenesis of amino acids 33-44 of the common α-subunit reveals different structural requirements for heterodimer expression among the glycoprotein hormones and suggests that cyclic adenosine 3',5'-monophosphate production and growth promotion are potentially dissociable functions of human thyrotropin
AUTHOR(S): Grossmann, Mathis; Szkudlinski, Mariusz W.; Dias, James A.; Xia, Haiying; Wong, Rosemary; Puett, David; Weintraub, Bruce D.
CORPORATE SOURCE: Natl. Inst. Diabetes Digestive Kidney Dis., Natl. Inst. Health, Bethesda, MD, 20892-1758, USA
SOURCE: Molecular Endocrinology (1996), 10(6), 769-779
CODEN: MOENEN; ISSN: 0888-8809
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Amino acid residues 33-44 of the common α-subunit of the glycoprotein hormones have been implicated in heterodimerization as well as high affinity receptor binding of human (h) CG. In the present study, we compared the role of specific amino acids within this region for glycoprotein hormone heterodimer formation, using a transient transfection system to coexpress different mutant α-subunit constructs with the β-subunit of either hTSH, hCG, or hFSH. Our results identified a crucial role for αPro38 in the heterodimer expression of hTSH as well as hFSH, similar to what had been described for hCG. In contrast, αAla36, which had been critical for hCG, was not essential for hTSH heterodimer expression and less important for hFSH, whereas αPhe33 and αArg35 appeared uniquely important for hFSH. Furthermore, we assessed the role of these residues for bioactivity and receptor binding of hTSH. Mutation of the surface-exposed residues αArg42-Ser43-Lys44, which form part of a unique α-helical structure, to Ala42-A;a43-Ala44, decreased TSH receptor binding using porcine thyroid membranes as well as rat FRTL-5 cells. Residues αPhe33 and αArg35, in contrast, were not important for high affinity binding of hTSH. In the signal transduction of hTSH, αAla36 was necessary for efficient growth induction in FRTL-5 cells but not for cAMP production in either FRTL-5 cells or Chinese hamster ovary cells expressing the human TSH receptor (JP09). Similarly, residues αArg42-Ser43-Lys44 were more important for hTSH-mediated induction of cell growth than cAMP production Mutating αArg35 to Ala reduced cAMP induction but not receptor binding of hTSH. In summary, using site-directed mutagenesis, we identified a domain, residues 33-44 of the common α-subunit, important in heterodimer expression, receptor

binding, and activation of hTSH. The comparison of the relative roles of specific amino acids within this region in hTSH with hCG and hFSH highlights previously unrecognized differences in the structural requirements for heterodimer expression among the members of the glycoprotein hormone family. Moreover, our findings revealed a novel role for residues α33-44 in triggering different postreceptor events, suggesting that cAMP production and growth promotion may, at least in part, be dissociable functions of hTSH.

OS.CITING REF COUNT: 23 THERE ARE 23 CAPLUS RECORDS THAT CITE THIS RECORD (23 CITINGS)

L3 ANSWER 8 OF 10 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:32955 BIOSIS
DOCUMENT NUMBER: PREV199698605090
TITLE: Expression of human thyrotropin in cell lines with different glycosylation patterns combined with mutagenesis of specific glycosylation sites: Characterization of a novel role for the oligosaccharides in the in vitro and in vivo bioactivity.
AUTHOR(S): Grossmann, Mathis [Reprint author]; Szkudlinski, Mariusz W.; Tropea, Joseph E.; Bishop, Leonora A.; Thotakura, N. Rao; Schofield, Peter R.; Weintraub, Bruce D.
CORPORATE SOURCE: Mol. Cellular Endocrinol. Branch, NIDDK, Natl. Inst. Health, Build. 10, Room 8 D14, Bethesda, MD 20892-1758, USA
SOURCE: Journal of Biological Chemistry, (1995) Vol. 270, No. 49, pp. 29378-29385.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jan 1996
Last Updated on STN: 27 Jan 1996

AB We used a novel approach to study the role of the Asn-linked oligosaccharides for human thyrotropin (hTSH) activity. Mutagenesis of Asn (N) within individual glycosylation recognition sequences to Gln (Q) was combined with expression of wild type and mutant hTSH in cell lines with different glycosylation patterns. The in vitro activity of hTSH lacking the Asn-alpha-52 oligosaccharide (alpha-Q52/TSH-beta) expressed in CHO-K1 cells (sialylated oligosaccharides) was increased 6-fold compared with wild type, whereas the activities of alpha-Q78/TSH-beta and alpha/TSH-beta-Q23 were increased 2-3-fold. Deletion of the Asn-alpha-52 oligosaccharide also increased the thyrotropic activity of human chorionic gonadotropin, in contrast to previous findings at its native receptor. The in vitro activity of wild type hTSH expressed in CHO-LEC2 cells (sialic acid-deficient oligosaccharides), CHO-LEC1 cells (Man-5GlcNAc-2 intermediates), and 293 cells (sulfated oligosaccharides) was 5-8-fold higher than of wild type from CHO-K1 cells. In contrast to CHO-K1 cells, there was no difference in the activity between wild type and selectively deglycosylated mutants expressed in these cell lines. Thus, in hTSH, the oligosaccharide at Asn-alpha-52 and, specifically, its terminal sialic acid residues attenuate in vitro activity, in contrast to the previously reported stimulatory role of this chain for human chorionic gonadotropin and human follitropin activity. The increased thyrotropic activity of alpha-Q52/CG-beta suggests that receptor-related mechanisms may be responsible for these differences among the glycoprotein hormones. Despite their increased in vitro activity, alpha-Q52/TSH-beta, and alpha-Q78/TSH-beta from CHO-K1 cells had a faster serum disappearance rate and decreased effect on T-4 production in mice. These findings highlight the importance of individual oligosaccharides in maintaining circulatory half-life and hence in vivo activity of hTSH.

L3 ANSWER 9 OF 10 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1996026861 MEDLINE

DOCUMENT NUMBER: PubMed ID: 7476992
TITLE: Role of the carboxy-terminal residues of the alpha-subunit in the expression and bioactivity of human thyroid-stimulating hormone.
AUTHOR: Grossmann M; Szkudlinski M W; Zeng H; Kraiem Z; Ji I; Tropea J E; Ji T H; Weintraub B D
CORPORATE SOURCE: Molecular and Cellular Endocrinology Branch, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland 20892-1758, USA.
CONTRACT NUMBER: HD-18702 (United States NICHD NIH HHS)
SOURCE: Molecular endocrinology (Baltimore, Md.), (1995 Aug) Vol. 9, No. 8, pp. 948-58.
Journal code: 8801431. ISSN: 0888-8809.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 24 Jan 1996
Last Updated on STN: 3 Feb 1997
Entered Medline: 6 Dec 1995

AB The glycoprotein hormones TSH, CG, LH, and FSH are heterodimers consisting of a hormone-specific beta-subunit and a common alpha-subunit. The aim of the present study was to investigate the role of the carboxy terminus of the common alpha-subunit (amino acids Tyr89-His90-Lys91-Ser92), which has been shown to be important for human (h) CG and hFSH, for the activity of hTSH. Successive truncations of the alpha-carboxy terminus by site-directed mutagenesis revealed a stepwise reduction of bioactivity occurring at residues alpha Ser92 and alpha His90 to 64% and 13%, respectively. This contrasts with previous findings for hCG and hFSH, where loss of bioactivity occurred in a single step with the deletion of alpha Lys91 but alpha Ser92 was not important. The decreased bioactivities of the hTSH alpha-truncation mutants were reflected by concomitant reductions of cAMP production, thyroid hormone synthesis and cell growth and were accompanied by a loss of receptor binding. Substitution of residues alpha Lys91 or alpha His90 with either a hydrophobic or a bulkier residues resulted in a reduction of receptor binding and signal transduction, indicating that the alpha-carboxy terminus of hTSH may interact with the TSH receptor in a tight contact area. Conversely, substitution of alpha His90 with smaller residues enhanced bioactivity. In addition, the integrity of the alpha-carboxy terminus was essential for hTSH expression. Thus, we showed common and different roles of the alpha-carboxy-terminal residues for the glycoprotein hormones. The unique role of alpha Ser92 in hTSH activity explains the evolutionary constraint to preserve the alpha-carboxy-terminal Ser92 in all glycoprotein hormones.

L3 ANSWER 10 OF 10 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 1992037350 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1935771
TITLE: The relationship between prorenin levels in follicular fluid and follicular atresia in bovine ovaries.
AUTHOR: Mukhopadhyay A K; Holstein K; Szkudlinski M; Brunswig-Spickenheier B; Leidenberger F A
CORPORATE SOURCE: Institute for Hormone and Fertility Research, Hamburg, Federal Republic of Germany.
SOURCE: Endocrinology, (1991 Nov) Vol. 129, No. 5, pp. 2367-75.
Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199112
ENTRY DATE: Entered STN: 24 Jan 1992
Last Updated on STN: 29 Jan 1999
Entered Medline: 2 Dec 1991

AB Bovine follicles having a higher concentration of progesterone than estradiol in the follicular fluid can be considered as atretic. Since we observed previously that there was an inverse relationship between the follicular fluid estradiol to progesterone (E/P) ratio and the prorenin level, we have proposed that a high prorenin level may be associated with follicular atresia. The aim of the present study was to corroborate this hypothesis by including additional indices to distinguish unambiguously between atretic and nonatretic follicles and to compare the prorenin levels in these two groups of follicles. The present study included examination of more than 200 follicles in the follicular fluid of which we have measured steroid and prorenin levels. The results obtained show a highly significant negative correlation between the prorenin level on the one hand and the E/P ratio, estrogen to total androgen ratio, or estradiol concentration on the other hand. As a further criterion for atresia, we have examined the histological characteristics of the follicles by light and electron microscopy and have found that 90% of histologically characterized atretic follicles had an E/P ratio less than 1 and an average prorenin level four to five times higher than nonatretic follicles. Finally, when we determined the FSH-stimulated cAMP response and the aromatase activity, in terms of the ability to convert exogenous androgen to estrogen in granulosa cells isolated from individual follicles, we observed a markedly higher prorenin level in the fluid of follicles whose granulosa cells responded poorly to FSH and showed a low aromatase activity, compared to follicles whose granulosa cells responded strongly to FSH and contained high aromatase activity. In summary, follicles that were classified as atretic on the basis of a number of biochemical and histological parameters contained significantly higher prorenin levels in their follicular fluid than nonatretic ones. Thus, a high follicular fluid prorenin level is a valid indicator for follicular atresia in bovine ovaries. However, the reason for this increase in follicular fluid prorenin level and whether this increase is a cause or a consequence of atresia remains to be determined.

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	44.07	44.29

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-3.28	-3.28

FILE 'STNGUIDE' ENTERED AT 15:10:20 ON 10 DEC 2009

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Dec 4, 2009 (20091204/UP).

=> dis ibib abs l6 1-34
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, BIOSIS, CAPLUS' - CONTINUE? (Y)/N:y

L6 ANSWER 1 OF 34 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:650039 BIOSIS
DOCUMENT NUMBER: PREV200600661389
TITLE: Follicle stimulating hormone superagonists.
AUTHOR(S): Anonymous; Szkudlinski, Mariusz W. [Inventor]; Weintraub, Bruce D. [Inventor]; Grossmann, Mathis [Inventor]
CORPORATE SOURCE: Potomac, MD USA
ASSIGNEE: The United States of America as represented by the Department of Health and Human Services
PATENT INFORMATION: US 07070788 20060704
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (JUL 4 2006)
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Nov 2006
Last Updated on STN: 29 Nov 2006

AB The invention is directed toward a human glycoprotein hormone having at least one, two, three, four, or five basic amino acids in the alpha-subunit at positions selected from the group consisting of positions 11, 13, 14, 16, 17, and 20. The inventions is also directed to a human glycoprotein where at least one of the amino acids at position 58, 63, and 69 of the beta-subunit of the human thyroid stimulating hormone are basic amino acids. The invention is further directed to a modified human glycoprotein hormone having increased activity over a wild-type human glycoprotein hormone, where the modified human glycoprotein comprises a basic amino acid substituted at a position corresponding to the same amino acid position in a non-human glycoprotein hormone having an increased activity over the wild-type human glycoprotein hormone. The invention is also directed to a method of constructing superactive nonchimeric analogs of human hormones comprising comparing the amino acid sequence of a more active homolog from another species to the human hormone, and selecting superactive analogs from the substituted human hormones. The invention is also directed to nucleic acids encoding the modified human glycoprotein hormones, vectors containing those nucleic acids, and host cells containing those vectors.

L6 ANSWER 2 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:1154787 CAPLUS
DOCUMENT NUMBER: 143:411096
TITLE: Human glycoprotein hormone superagonists and uses thereof
INVENTOR(S): Szkudlinski, Mariusz W.; Weintraub, Bruce D.
PATENT ASSIGNEE(S): Trophogen, Inc., USA
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005101000	A2	20051027	WO 2005-US8957	20050318
WO 2005101000	A3	20061123		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM,
SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

AU 2005233923	A1	20051027	AU 2005-233923		20050318
CA 2561545	A1	20051027	CA 2005-2561545		20050318
EP 1738174	A2	20070103	EP 2005-732628		20050318
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU					
CN 1965234	A	20070516	CN 2005-80017466		20050318
BR 2005009469	A	20070911	BR 2005-9469		20050318
JP 2007530974	T	20071101	JP 2007-506215		20050318
US 20090214424	A1	20090827	US 2006-594843		20060928
MX 2006011290	A	20070321	MX 2006-11290		20060929
IN 2006KN03161	A	20070608	IN 2006-KN3161		20061030
PRIORITY APPLN. INFO.:			US 2004-557704P	P	20040331
			WO 2005-US8957	W	20050318

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The present invention provides improved methods of imaging, targeted therapy and detection and diagnostics using modified glycoprotein hormones having increased activity over wild-type hormones. The methods involve assaying for an analyte that interferes with the binding of a modified glycoprotein hormone to a glycoprotein hormone receptor. Targeted delivery of therapeutic agents coupled to a modified glycoprotein hormone is also claimed.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:1049828 CAPLUS
DOCUMENT NUMBER: 143:339960
TITLE: Follicle-stimulating hormone superagonists with improved potency, pharmacokinetics and plasma half-life
INVENTOR(S): Szkudlinski, Mariusz W.; Weintraub, Bruce D.
PATENT ASSIGNEE(S): Trophogen, Inc., USA
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005089445	A2	20050929	WO 2005-US8960	20050318
WO 2005089445	A3	20080221		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,

MR, NE, SN, TD, TG, AP, EA, EP, OA

AU 2005223651	A1	20050929	AU 2005-223651	20050318
CA 2563345	A1	20050929	CA 2005-2563345	20050318
EP 1734979	A2	20061227	EP 2005-732601	20050318
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
US 20070219116	A1	20070920	US 2006-593466	20060919
MX 2006011898	A	20080613	MX 2006-11898	20061013
IN 2006KN03017	A	20070608	IN 2006-KN3017	20061018
CN 101189259	A	20080528	CN 2005-80015850	20061117
PRIORITY APPLN. INFO.:			US 2004-554419P P	20040319
			WO 2005-US8960 W	20050318

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB This invention provides superactive analogs of FSH demonstrating enhanced bioactivity both in vitro and in vivo as compared to wild type FSH. In particular, the analogs of the invention demonstrate at least a 10-fold increase in potency or at least a 10% increase in maximal efficacy as compared to wild type protein. Preferred α-subunit mutations comprise at least two basic amino acids at positions corresponding to positions 13, 14, 16, 17, 20, 21,22, 66, 68, 73,74, and 81, and a modified β-subunit comprises at least one basic amino acid at a position corresponding to any one of positions 2,4,14,63,64, 67, and 69. Sequences providing potential glycosylation recognition sites may be either an N-terminal or C-terminal extension on either the α or β chain. One of the analogs of the invention (designated TR-4402) comprises the substitutions α(E14R+Q20R+Q20R) + β(E4R). The analogs are particularly useful for treating subjects showing low FSH receptor expression or poor FSH receptor responsiveness, and for the treatment of any condition associated with glycoprotein hormone activity.

L6 ANSWER 4 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:	1997:746157 CAPLUS
DOCUMENT NUMBER:	128:19051
ORIGINAL REFERENCE NO.:	128:3634h,3635a
TITLE:	Glycoprotein hormone superagonists, their preparation with recombinant cells, and their use in treatment of diseases and dysfunctions
INVENTOR(S):	Szkudlinski, Mariusz W.; Weintraub, Bruce D. ; Grossman, Mathis
PATENT ASSIGNEE(S):	United States Dept. of Health and Human Services, USA; Szkudlinski, Mariusz W.; Weintraub, Bruce D.; Grossman, Mathis
SOURCE:	PCT Int. Appl., 90 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9742322	A1	19971113	WO 1996-US6483	19960508
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2253441	A1	19971113	CA 1996-2253441	19960508

AU 9658549	A	19971126	AU 1996-58549	19960508
AU 714635	B2	20000106		
EP 954578	A1	19991110	EP 1996-920151	19960508
EP 954578	B1	20071219		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 2000509603	T	20000802	JP 1997-539866	19960508
JP 3981413	B2	20070926		
AT 381617	T	20080115	AT 1996-920151	19960508
EP 1947117	A2	20080723	EP 2007-150018	19960508
EP 1947117	A3	20081008		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US 6361992	B1	20020326	US 1998-185408	19981103
KR 2000010866	A	20000225	KR 1998-709010	19981107
US 20020110909	A1	20020815	US 2002-57113	20020125
US 7070788	B2	20060704		
US 20060183672	A1	20060817	US 2006-409428	20060421
JP 2007259860	A	20071011	JP 2007-124785	20070509
JP 4081130	B2	20080423		
JP 2008079619	A	20080410	JP 2007-317316	20071207
US 20090233846	A1	20090917	US 2009-467081	20090515

PRIORITY APPLN. INFO.:	EP 1996-920151	A3 19960508
	JP 1997-539866	A3 19960508
	WO 1996-US6483	A 19960508
	US 1998-185408	A3 19981103
	US 2002-57113	A1 20020125
	US 2006-409428	A3 20060421
	JP 2007-124785	A3 20070509

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention is directed toward a human glycoprotein hormone having at least one, two, three, four or five basic amino acids in the α-subunit at positions selected from the group consisting of positions 11, 13, 14, 16, 17 and 20. The invention is also directed to a human glycoprotein where at least one of the amino acids at positions 58, 63 and 69 of the β-subunit of the human TSH are basic amino acids. The invention is also directed to a method of constructing superactive nonchimeric analogs of human hormones comprising comparing the amino acid sequence of a more active homolog from another species to the human hormone, substituting selected amino acids in the human hormone with the corresponding amino acids from the other species, determining the activity of the substituted human hormones, and selecting superactive analogs from the substituted human hormones. The invention is also directed to nucleic acids encoding the modified human glycoprotein hormones, vectors containing those nucleic acids, and host cells containing those vectors. The superagonists may be used in treatment of diseases such as thyroid carcinoma and disfunctions such as infertility. Multiply substituted human TSH (i.e., A13K, P16K and Q20K in the α subunit and L69R in the β subunit) displayed a 95.7-fold increase in potency relative to wild-type TSH.

OS.CITING REF COUNT:	7	THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT:	2	THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 34 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER:	1997407919 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 9261143
TITLE:	Human thyroid-stimulating hormone (hTSH) subunit gene fusion produces hTSH with increased stability and serum half-life and compensates for mutagenesis-induced defects in subunit association.
AUTHOR:	Grossmann M; Wong R; Szkudlinski M W; Weintraub B D
CORPORATE SOURCE:	Department of Medicine, University of Maryland School of

Medicine and the Institute of Human Virology, Medical Biotechnology Center, Baltimore, Maryland 21201, USA.. grossman@umbi.umd.edu
SOURCE: The Journal of biological chemistry, (1997 Aug 22) Vol. 272, No. 34, pp. 21312-6.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 26 Sep 1997
Last Updated on STN: 26 Sep 1997
Entered Medline: 15 Sep 1997
AB The human thyroid-stimulating hormone (hTSH) subunits alpha and beta are transcribed from different genes and associate noncovalently to form the bioactive hTSH heterodimer. Dimerization is rate-limiting for hTSH secretion, and dissociation leads to hormone inactivation. Previous studies on human chorionic gonadotropin (hCG) and human follicle -stimulating hormone had shown that it was possible by subunit gene fusion to produce a bioactive, single chain hormone. However, neither the stability nor the clearance from the circulation of such fused glycoprotein hormones has been studied. We show here that genetic fusion of the hTSH alpha- and beta-subunits using the carboxyl-terminal peptide of the hCG beta-subunit as a linker created unimolecular hTSH whose receptor binding and bioactivity were comparable to native hTSH. Interestingly, the fused hTSH had higher thermostability and a longer plasma half-life than either native or dimeric hTSH containing the hCG beta-subunit-carboxyl-terminal peptide, suggesting that dimer dissociation may contribute to glycoprotein hormone inactivation in vivo. In addition, we show for the first time that synthesis of hTSH as a single polypeptide chain could overcome certain mutagenesis-induced defects in hTSH secretion, therefore enabling functional studies of such mutants. Thus, in addition to prolongation of plasma half-life, genetic fusion of hTSH subunits should be particularly relevant for the engineering of novel analogs where desirable features are offset by decreased dimer formation or stability. Such methods provide a general approach to expand the spectrum of novel recombinant glycoprotein hormones available for in vitro and in vivo study.

L6 ANSWER 6 OF 34 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1997326138 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9182589
TITLE: Substitution of the seat-belt region of the thyroid-stimulating hormone (TSH) beta-subunit with the corresponding regions of choriogonadotropin or follitropin confers luteotropic but not follitropic activity to chimeric TSH.
AUTHOR: Grossmann M; Szkudlinski M W; Wong R; Dias J A; Ji T H; Weintraub B D
CORPORATE SOURCE: Laboratory of Molecular Endocrinology, Department of Medicine, University of Maryland School of Medicine and the Institute of Human Virology, Medical Biotechnology Center, Baltimore, Maryland 21201, USA.. grossman@umbi.umd.edu
SOURCE: The Journal of biological chemistry, (1997 Jun 13) Vol. 272, No. 24, pp. 15532-40.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707

ENTRY DATE: Entered STN: 24 Jul 1997
Last Updated on STN: 24 Jul 1997
Entered Medline: 14 Jul 1997

AB The region between the 10th and 12th cysteine (Cys88-Cys105 in human thyroid-stimulating hormone beta-subunit (hTSHbeta)) of the glycoprotein hormone beta-subunits corresponds to the disulfide-linked seat-belt region. It wraps around the common alpha-subunit and has been implicated in regulating specificity between human choriogonadotropin (hCG) and human follicle-stimulating hormone (hFSH), but determinants of hTSH specificity are unknown. To characterize the role of this region for hTSH, we constructed hTSH chimeras in which the entire seat-belt region Cys88-Cys105 or individual intercysteine segments Cys88-Cys95 and Cys95-Cys105 were replaced with the corresponding sequences of hCG and hFSH or alanine cassettes. Alanine cassette mutagenesis of hTSH showed that the Cys95-Cys105 segment of the seat-belt was more important for TSH receptor binding and signal transduction than the Cys88-Cys95 determinant loop region. Replacing the entire seat-belt of hTSHbeta with the hCG sequence conferred full hCG receptor binding and activation to the hTSH chimera, whereas TSH receptor binding and activation were abolished. Conversely, introduction of the hTSHbeta seat-belt sequence into hCGbeta generated an hCG chimera that bound to and activated the TSH receptor but not the CG/lutropin (LH) receptor. In contrast, an hTSH chimera bearing hFSH seat-belt residues did not possess any follitropic activity, and its thyrotropic activity was only slightly reduced. This may in part be due to the fact that the net charge of the seat-belt is similar in hTSH and hFSH but different from hCG. However, exchanging other regions of charge heterogeneity between hTSHbeta and hFSHbeta did not confer follitropic activity to hTSH. Thus, exchanging the seat-belt region between hTSH and hCG switches hormonal specificity in a mutually exclusive fashion. In contrast, the seat-belt appears not to discriminate between the TSH and the FSH receptors, indicating for the first time that domains outside the seat-belt region contribute to glycoprotein hormone specificity.

L6 ANSWER 7 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:340938 CAPLUS
DOCUMENT NUMBER: 125:26466
ORIGINAL REFERENCE NO.: 125:4999a,5002a
TITLE: Site-directed mutagenesis of amino acids 33-44 of the common α-subunit reveals different structural requirements for heterodimer expression among the glycoprotein hormones and suggests that cyclic adenosine 3',5'-monophosphate production and growth promotion are potentially dissociable functions of human thyrotropin
AUTHOR(S): Grossmann, Mathis; Szkudlinski, Mariusz W.; Dias, James A.; Xia, Haiying; Wong, Rosemary; Puett, David; Weintraub, Bruce D.
CORPORATE SOURCE: Natl. Inst. Diabetes Digestive Kidney Dis., Natl. Inst. Health, Bethesda, MD, 20892-1758, USA
SOURCE: Molecular Endocrinology (1996), 10(6), 769-779
CODEN: MOENEN; ISSN: 0888-8809
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Amino acid residues 33-44 of the common α-subunit of the glycoprotein hormones have been implicated in heterodimerization as well as high affinity receptor binding of human (h) CG. In the present study, we compared the role of specific amino acids within this region for glycoprotein hormone heterodimer formation, using a transient transfection system to coexpress different mutant α-subunit constructs with the β-subunit of either hTSH, hCG, or hFSH. Our results identified a

crucial role for αPro38 in the heterodimer expression of hTSH as well as hFSH, similar to what had been described for hCG. In contrast, αAla36, which had been critical for hCG, was not essential for hTSH heterodimer expression and less important for hFSH, whereas αPhe33 and αArg35 appeared uniquely important for hFSH. Furthermore, we assessed the role of these residues for bioactivity and receptor binding of hTSH. Mutation of the surface-exposed residues αArg42-Ser43-Lys44, which form part of a unique α-helical structure, to Ala42-A;a43-Ala44, decreased TSH receptor binding using porcine thyroid membranes as well as rat FRTL-5 cells. Residues αPhe33 and αArg35, in contrast, were not important for high affinity binding of hTSH. In the signal transduction of hTSH, αAla36 was necessary for efficient growth induction in FRTL-5 cells but not for cAMP production in either FRTL-5 cells or Chinese hamster ovary cells expressing the human TSH receptor (JP09). Similarly, residues αArg42-Ser43-Lys44 were more important for hTSH-mediated induction of cell growth than cAMP production Mutating αArg35 to Ala reduced cAMP induction but not receptor binding of hTSH. In summary, using site-directed mutagenesis, we identified a domain, residues 33-44 of the common α-subunit, important in heterodimer expression, receptor binding, and activation of hTSH. The comparison of the relative roles of specific amino acids within this region in hTSH with hCG and hFSH highlights previously unrecognized differences in the structural requirements for heterodimer expression among the members of the glycoprotein hormone family. Moreover, our findings revealed a novel role for residues α33-44 in triggering different postreceptor events, suggesting that cAMP production and growth promotion may, at least in part, be dissociable functions of hTSH.

OS.CITING REF COUNT: 23 THERE ARE 23 CAPLUS RECORDS THAT CITE THIS RECORD (23 CITINGS)

L6 ANSWER 8 OF 34 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:45646 BIOSIS
DOCUMENT NUMBER: PREV199598059946
TITLE: Cloning and regulation of glycoprotein hormone receptor genes.
AUTHOR(S): Kohn, Leornard D.; Ban, Toshiaki; Okajima, Fumikazu; Shimura, Hiroki; Shimura, Yoshie; Hidaka, Akinari; Giuliani, Cesidio; Napolitano, Giorgio; Kosugi, Shinji; Ikuyama, Shoichiro; Akamizu, Takashi; Tahara, Kazuo; Saji, Motoyasu
CORPORATE SOURCE: Lab. Biochemistry Metabolism, National Inst. Diabetes Digestive Kidney Diseases, National Inst. Health, Building 10, Bethesda, MD 20892, USA
SOURCE: Weintraub, B. D. [Editor]. (1995) pp. 133-153.
Molecular endocrinology: Basic concepts and clinical correlations.
Publisher: Raven Press, 1185 Avenue of the Americas, New York, New York 10036-2806, USA.
ISBN: 0-7817-0223-2.
DOCUMENT TYPE: Book
Book; (Book Chapter)
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Jan 1995
Last Updated on STN: 1 Feb 1995

L6 ANSWER 9 OF 34 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:32955 BIOSIS
DOCUMENT NUMBER: PREV199698605090
TITLE: Expression of human thyrotropin in cell lines with different glycosylation patterns combined with mutagenesis of specific glycosylation sites: Characterization of a

novel role for the oligosaccharides in the in vitro and in vivo bioactivity.

AUTHOR(S): Grossmann, Mathis [Reprint author]; Szkudlinski, Mariusz W.; Tropea, Joseph E.; Bishop, Leonora A.; Thotakura, N. Rao; Schofield, Peter R.; Weintraub, Bruce D.

CORPORATE SOURCE: Mol. Cellular Endocrinol. Branch, NIDDK, Natl. Inst. Health, Build. 10, Room 8 D14, Bethesda, MD 20892-1758, USA

SOURCE: Journal of Biological Chemistry, (1995) Vol. 270, No. 49, pp. 29378-29385.
CODEN: JBCHA3. ISSN: 0021-9258.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 26 Jan 1996
Last Updated on STN: 27 Jan 1996

AB We used a novel approach to study the role of the Asn-linked oligosaccharides for human thyrotropin (hTSH) activity. Mutagenesis of Asn (N) within individual glycosylation recognition sequences to Gln (Q) was combined with expression of wild type and mutant hTSH in cell lines with different glycosylation patterns. The in vitro activity of hTSH lacking the Asn-alpha-52 oligosaccharide (alpha-Q52/TSH-beta) expressed in CHO-K1 cells (sialylated oligosaccharides) was increased 6-fold compared with wild type, whereas the activities of alpha-Q78/TSH-beta and alpha/TSH-beta-Q23 were increased 2-3-fold. Deletion of the Asn-alpha-52 oligosaccharide also increased the thyrotropic activity of human chorionic gonadotropin, in contrast to previous findings at its native receptor. The in vitro activity of wild type hTSH expressed in CHO-LEC2 cells (sialic acid-deficient oligosaccharides), CHO-LEC1 cells (Man-5GlcNAc-2 intermediates), and 293 cells (sulfated oligosaccharides) was 5-8-fold higher than of wild type from CHO-K1 cells. In contrast to CHO-K1 cells, there was no difference in the activity between wild type and selectively deglycosylated mutants expressed in these cell lines. Thus, in hTSH, the oligosaccharide at Asn-alpha-52 and, specifically, its terminal sialic acid residues attenuate in vitro activity, in contrast to the previously reported stimulatory role of this chain for human chorionic gonadotropin and human follitropin activity. The increased thyrotropic activity of alpha-Q52/CG-beta suggests that receptor-related mechanisms may be responsible for these differences among the glycoprotein hormones. Despite their increased in vitro activity, alpha-Q52/TSH-beta, and alpha-Q78/TSH-beta from CHO-K1 cells had a faster serum disappearance rate and decreased effect on T-4 production in mice. These findings highlight the importance of individual oligosaccharides in maintaining circulatory half-life and hence in vivo activity of hTSH.

L6 ANSWER 10 OF 34 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER: 1996026861 MEDLINE

DOCUMENT NUMBER: PubMed ID: 7476992

TITLE: Role of the carboxy-terminal residues of the alpha-subunit in the expression and bioactivity of human thyroid-stimulating hormone.

AUTHOR: Grossmann M; Szkudlinski M W; Zeng H; Kraiem Z; Ji I; Tropea J E; Ji T H; Weintraub B D

CORPORATE SOURCE: Molecular and Cellular Endocrinology Branch, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland 20892-1758, USA.

CONTRACT NUMBER: HD-18702 (United States NICHD NIH HHS)

SOURCE: Molecular endocrinology (Baltimore, Md.), (1995 Aug) Vol. 9, No. 8, pp. 948-58.
Journal code: 8801431. ISSN: 0888-8809.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)

(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 24 Jan 1996
Last Updated on STN: 3 Feb 1997
Entered Medline: 6 Dec 1995

AB The glycoprotein hormones TSH, CG, LH, and FSH are heterodimers consisting of a hormone-specific beta-subunit and a common alpha-subunit. The aim of the present study was to investigate the role of the carboxy terminus of the common alpha-subunit (amino acids Tyr89-His90-Lys91-Ser92), which has been shown to be important for human (h) CG and hFSH, for the activity of hTSH. Successive truncations of the alpha-carboxy terminus by site-directed mutagenesis revealed a stepwise reduction of bioactivity occurring at residues alpha Ser92 and alpha His90 to 64% and 13%, respectively. This contrasts with previous findings for hCG and hFSH, where loss of bioactivity occurred in a single step with the deletion of alpha Lys91 but alpha Ser92 was not important. The decreased bioactivities of the hTSH alpha-truncation mutants were reflected by concomitant reductions of cAMP production, thyroid hormone synthesis and cell growth and were accompanied by a loss of receptor binding. Substitution of residues alpha Lys91 or alpha His90 with either a hydrophobic or a bulkier residues resulted in a reduction of receptor binding and signal transduction, indicating that the alpha-carboxy terminus of hTSH may interact with the TSH receptor in a tight contact area. Conversely, substitution of alpha His90 with smaller residues enhanced bioactivity. In addition, the integrity of the alpha-carboxy terminus was essential for hTSH expression. Thus, we showed common and different roles of the alpha-carboxy-terminal residues for the glycoprotein hormones. The unique role of alpha Ser92 in hTSH activity explains the evolutionary constraint to preserve the alpha-carboxy-terminal Ser92 in all glycoprotein hormones.

L6 ANSWER 11 OF 34 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 1988087762 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3121663
TITLE: Comparison of the effects of lung cancer, benign lung disease, and normal aging on pituitary-gonadal function in men.
AUTHOR: Blackman M R; Weintraub B D; Rosen S W; Harman S M
CORPORATE SOURCE: Department of Medicine, Francis Scott Key Medical Center, National Institute on Aging, Baltimore, Maryland 21224.
SOURCE: The Journal of clinical endocrinology and metabolism, (1988 Jan) Vol. 66, No. 1, pp. 88-95.
Journal code: 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198802
ENTRY DATE: Entered STN: 5 Mar 1990
Last Updated on STN: 5 Mar 1990
Entered Medline: 2 Feb 1988

AB We retrospectively determined serum total testosterone (T), fraction of T bound, free T index, LH, and FSH levels in 122 men with malignant lung disease, 32 men with benign lung disease, and 106 normal men. Men with malignant and, to a lesser extent, benign lung disease had decreased serum total T and free T index values at the 5th percentiles, with elevations of LH and FSH levels at the 95th percentiles. Linear regression analysis showed reductions in total T and free T index

and increases in FSH, but not LH, levels with age in each group. Using multivariate analysis, we found stronger independent effects of disease than age on serum total T and fraction of T bound, but a greater influence of age on free T index. Serum LH values differed by diagnosis, whereas FSH differed by age. Relative to values in the normal men, mean serum total T levels were reduced in men with lung cancer; the fraction of T bound was decreased in the men with lung cancer and increased in the men with benign lung disease, the free T index was decreased in the men with both malignant and benign lung disease, and LH was increased in the men with lung cancer. The hormone and hormone binding results were similar in men with different types of lung cancer. Biochemical evidence of primary and secondary (or combined primary and secondary) hypogonadism was present in 50-59% and 28-32%, respectively, of the men with malignant and benign lung disease vs. 10% of the normal men. These data suggest that 1) there is an increased prevalence of both pituitary gonadotropic and testicular dysfunction in men with malignant and, to a lesser extent, benign chronic lung disease, and 2) the effects of illness are independent of, and quantitatively greater than, those due to age.

L6 ANSWER 12 OF 34 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 1987053588 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3096695
TITLE: Differences in the carbohydrate moieties of the common alpha-subunits of human chorionic gonadotropin, luteinizing hormone, follicle-stimulating hormone, and thyrotropin: preliminary structural inferences from direct methylation analysis.
AUTHOR: Nilsson B; Rosen S W; Weintraub B D; Zopf D A
SOURCE: Endocrinology, (1986 Dec) Vol. 119, No. 6, pp. 2737-43. Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198612
ENTRY DATE: Entered STN: 2 Mar 1990
Last Updated on STN: 2 Mar 1990
Entered Medline: 24 Dec 1986

AB The carbohydrate components of combined alpha-subunits of urinary hCG and human pituitary LH (hLH), FSH (hFSH), and TSH (hTSH), each derived from the intact hormone, were studied by direct sugar analysis and methylation analysis. The methods provide a complete survey of the structural elements contained in the complex sugars associated with these glycoproteins, but do not establish the sugar sequences or anomeric configurations of glycosidic bonds. By analogy to N-linked oligosaccharides that occur in many glycoproteins, the data suggest distinct structural features for carbohydrates of alpha-subunits combined with beta-subunits. hCG alpha contains biantennary asparagine-linked chains terminated by either NeuAc alpha 2-3Gal beta 1- or GlcNAc beta 1-2 Man alpha 1- and lacks fucose. hTSH alpha contains biantennary chains with the same termini as hCG alpha plus terminal R-O-4GalNAc and a fucosyl residue linked alpha 1-6 to the inner GlcNAc residue of the N-linked chitobiosyl core. hLH alpha may contain some high mannose chains, but primarily contains biantennary chains terminated by NeuAc alpha 2-3(6)Gal beta 1-, GlcNAc beta 1-, GalNac-1-, R'-O-6GlcNAc-1-, and R"-0-2Man-1-plus a fucosyl residue linked alpha 1-6 to the inner GlcNAc residue of the N-linked chitobiosyl core. hFSH alpha contains more complicated structures that probably include a bisecting GlcNAc residue linked beta 1-4 to a 3,6-di-O-substituted core mannosyl residue, and terminal NeuAc alpha 2-3Gal beta 1-4(+/- Fuc alpha 1-3)GlcNAc-1, Gal beta 1-4(+/- Fuc alpha 1-3)GlcNAc-1-, R"'-O-GalNAc-1-, and GalNAc-1. In addition, the presence

of 2,4-di-O-substituted mannose in hFSH alpha indicates that it contains triantennary chains. The identities of the R; R', R", and R"' groups were not determined, but recent studies of glycoprotein hormones suggest that they may be sulfate groups. Our results demonstrate differential glycosylation of virtually identical polypeptide hormone alpha-subunits produced in the same organ or perhaps even in the same cell.

L6 ANSWER 13 OF 34 MEDLINE on STN
ACCESSION NUMBER: 1982214393 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6806313
TITLE: Recovery of pituitary secretion of thyrotropin and its free alpha- and beta-subunits after triiodothyronine withdrawal.
AUTHOR: Goldman J M; Weintraub B D
SOURCE: The Journal of clinical endocrinology and metabolism, (1982 Aug) Vol. 55, No. 2, pp. 337-40.
Journal code: 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198208
ENTRY DATE: Entered STN: 17 Mar 1990
Last Updated on STN: 17 Mar 1990
Entered Medline: 14 Aug 1982

L6 ANSWER 14 OF 34 MEDLINE on STN
ACCESSION NUMBER: 1981238325 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6166541
TITLE: Ectopic production in serum-free media of the common alpha subunit of the glycoprotein hormones.
AUTHOR: Morrow J S; Weintraub B C; Rosen S W
SOURCE: In vitro, (1981 May) Vol. 17, No. 5, pp. 421-6.
Journal code: 0063733. ISSN: 0073-5655.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198109
ENTRY DATE: Entered STN: 16 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 22 Sep 1981
AB The HeLa-S3 cell strain grown in Ham's F12 medium supplemented with insulin, transferrin, cortisol, epidermal growth factor, fibroblast growth factor, and trace elements, but containing no serum, continued to produce the common alpha-subunit of the glycoprotein hormones for the 10 d study. The amounts of alpha-subunit secreted into the medium during the first 4 d were indistinguishable from those in F12 medium supplemented with 10% fetal bovine serum. During the remainder of the experiment the amounts of alpha-subunit reached 50 to 80% those in the serum-supplemented medium.

L6 ANSWER 15 OF 34 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 1981215876 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6165733
TITLE: Discordant elevation of the common alpha-subunit of the glycoprotein hormones compared to beta-subunits in serum of uremic patients.
AUTHOR: Blackman M R; Weintraub B D; Kourides I A; Solano J T; Santner T; Rosen S W
CONTRACT NUMBER: AM-00679 (United States NIADDK NIH HHS)
CA-08748 (United States NCI NIH HHS)
CA-23185 (United States NCI NIH HHS)
SOURCE: The Journal of clinical endocrinology and metabolism, (1981

Jul) Vol. 53, No. 1, pp. 39-48.
Journal code: 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198108
ENTRY DATE: Entered STN: 16 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 20 Aug 1981

L6 ANSWER 16 OF 34 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 1980156552 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6767594
TITLE: Purification of thyrotropin and other glycoprotein hormones by immunoaffinity chromatography.
AUTHOR: Pekonen F; Williams D M; Weintraub B D
SOURCE: Endocrinology, (1980 May) Vol. 106, No. 5, pp. 1327-32.
Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198006
ENTRY DATE: Entered STN: 15 Mar 1990
Last Updated on STN: 15 Mar 1990
Entered Medline: 27 Jun 1980

L6 ANSWER 17 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 1980:424025 CAPLUS
DOCUMENT NUMBER: 93:24025
ORIGINAL REFERENCE NO.: 93:4045a,4048a
TITLE: Nonrandom ectopic protein production by malignant cells: direct evidence in vitro
AUTHOR(S): Rosen, Saul W.; Weintraub, Bruce D.; Aaronson, Stuart A.
CORPORATE SOURCE: Clin. Endocrinol. Branch, Natl. Inst. Arthritis, Metab. Dig. Dis., Bethesda, MD, 20205, USA
SOURCE: Journal of Clinical Endocrinology and Metabolism (1980), 50(5), 834-41
CODEN: JCEMAZ; ISSN: 0021-972X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cell lines derived from malignant human neoplasms (21 carcinomas or melanomas and 11 sarcomas or gliomas) and 18 human fibroblast lines were examined for ectopic protein production Thirteen malignant lines produced ectopic chorionic gonadotropin (CG) or its β-subunit (0.5-5.6 pmol/mg cell protein/24 h). Four malignant lines produced ectopic carcinoembryonic antigen (0.04-0.95pmol/mg cell protein/24 h), whereas none produced placental lactogen or α-fetoprotein. Six malignant lines produced ectopically the common α-subunit of the glycoprotein hormones, and in 2 (ChaGo lung and Chang liver), the secretion rates (391 and 506 pmol/mg cell protein/24 h) were almost 100 times higher than that of any other ectopic protein. Eight malignant lines produced low levels of prolactin (PRL)(0.1-0.57 pmol/mg cell protein/24 h) and 3 lines produced low levels of LH or its β-subunit (0.1-0.26pmol/mg cell protein/24 h), but neither was secreted. In contrast, only 2 normal fibroblast lines produced CG, and 1 produced PRL-like activity. None of the malignant or fibroblast lines produced GH or FSH or its β-subunit. Moreover, no line produced cortisol, progesterone,

17α-hydroxyprogesterone, testosterone, or aldosterone. Estrone and estradiol were found in the media from 4 malignant lines (1.1-9.4 pmol/mg protein). Apparently, ectopic protein production is widely prevalent in malignant cells in culture and rare in normal fibroblast cultures, is nonrandom, with large amts. of certain proteins but undetectable amts. of others, and is underestd. by criteria of serum concentration alone, since certain lines produce low levels or do not secrete. The multiple enzymes required for steroidogenesis are not produced together ectopically, but estrogen production by cells in media containing serum may require only a single aromatase or desulfurylase.

OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (12 CITINGS)

L6 ANSWER 18 OF 34 MEDLINE on STN DUPLICATE 9

ACCESSION NUMBER: 1980200390 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6769614
TITLE: Excess free alpha relative to beta subunits of the glycoprotein hormones in normal and abnormal human pituitary glands.
AUTHOR: Kourides I A; Landon M B; Hoffman B J; Weintraub B D
SOURCE: Clinical endocrinology, (1980 Apr) Vol. 12, No. 4, pp. 407-16.
Journal code: 0346653. ISSN: 0300-0664.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198008
ENTRY DATE: Entered STN: 15 Mar 1990
Last Updated on STN: 15 Mar 1990
Entered Medline: 25 Aug 1980

L6 ANSWER 19 OF 34 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 10

ACCESSION NUMBER: 1980:198705 BIOSIS
DOCUMENT NUMBER: PREV198069073701; BA69:73701
TITLE: INTERACTION OF CRUDE AND PURE CHORIONIC GONADOTROPIN WITH THE THYROTROPIN RECEPTOR.
AUTHOR(S): PEKONEN F [Reprint author]; WEINTRAUB B D
CORPORATE SOURCE: NATL INST HEALTH, BUILD 10, ROOM 8N 315, BETHESDA, MD 20205, USA
SOURCE: Journal of Clinical Endocrinology and Metabolism, (1980) Vol. 50, No. 2, pp. 280-285.
CODEN: JCEMAZ. ISSN: 0021-972X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB The effect of crude and pure hCG [human chorionic gonadotropin] preparations on bovine [b] TSH [thyrotropin] binding to its receptor was investigated in an attempt to further characterize the intrinsic thyrotropic activity of hCG. In a TSH radioreceptor assay with bovine thyroid membranes performed at 4° C without NaCl in the incubation medium, the cross-reactivity of a crude hCG preparation was 90% relative to unlabeled bTSH, whereas that of pure hCG and its subunits was below 0.01%. By Sephadex G-100 chromatography, the substances in crude hCG that displayed TSH binding inhibitory activity at 4° C exhibited great heterogeneity, with an apparent molecular size range of 6000-70,000

daltons. No specific peaks of TSH binding inhibitory substances were observed in the elution region of hCG, TSH, or molar or chorionic TSH, and most of the inhibitory substances had apparent molecular sizes smaller than any known TSH. When the radioreceptor assay was performed under progressively more physiological conditions by raising the temperature to 37° C and adding NaCl to the incubation buffer, the cross-reactivity of crude and pure hCG relative to bTSH fell to 0.003-0.005% both with bovine and human thyroid membranes. The similar effects of crude and pure hCG under near physiological incubation conditions suggested that the active substance in the crude hCG preparation was hCG, whereas the effect of the other substances in the preparation had been abolished. Under such conditions, no cross-reactivity of hCG subunits was observed, whereas the cross-reactivity of human TSH was 10%, that of human LH [lutropin] was 0.3% and that of human FSH [follitropin] was 0.1% relative to bTSH. Based on the TSH radioreceptor assay performed under near physiological incubation conditions, resulting in maximal TSH sensitivity and specificity, the thyrotropic activity of 1 IU (gonadotropic activity) of hCG is thus equivalent to 0.05-0.08 μIU bTSH.

L6 ANSWER 20 OF 34 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 1980230517 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6248674
TITLE: Human placental and pituitary glycoprotein hormones and their subunits as tumor markers: a quantitative assessment.
AUTHOR: Blackman M R; Weintraub B D; Rosen S W; Kourides I A; Steinwascher K; Gail M H
SOURCE: Journal of the National Cancer Institute, (1980 Jul) Vol. 65, No. 1, pp. 81-93.
Journal code: 7503089. ISSN: 0027-8874.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198009
ENTRY DATE: Entered STN: 15 Mar 1990
Last Updated on STN: 15 Mar 1990
Entered Medline: 28 Sep 1980

L6 ANSWER 21 OF 34 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 1979148214 MEDLINE
DOCUMENT NUMBER: PubMed ID: 34508
TITLE: Thyrotropin binding to cultured lymphocytes and thyroid cells.
AUTHOR: Pekonen F; Weintraub B D
SOURCE: Endocrinology, (1978 Nov) Vol. 103, No. 5, pp. 1668-77.
Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197906
ENTRY DATE: Entered STN: 15 Mar 1990
Last Updated on STN: 6 Feb 1995
Entered Medline: 29 Jun 1979
AB The TSH-binding properties of human lymphocytes in continuous culture were studied and compared to those of bovine and human thyroid cells in primary culture. Both lymphocytes and thyroid cells had maximal TSH-binding capacity at pH 5.2. At pH 7.4, thyroid cells bound 15% but lymphocytes bound only 3% of the amount bound at pH 5.2. At 37 C, maximal binding of

[125I]iodo-TSH to lymphocytes was reached within 60--90 min and maximal binding to thyroid cells was reached within 15--20 min. TSH binding to lymphocytes was salt sensitive, being inhibited to 50% by 0.2 mM MgCl and 0.4 mM CaCl2 and by 20 mM Kl, KCl, and NaCl. The saturable binding of bovine TSH (bTSH) to thyroid cells at pHs 5.2 and 7.4 was above 90% of the total binding. Saturable binding of bovine TSH (bTSH) to thyroid cells at pHs 5.2 and 7.4 was above 90% of the total binding. Saturable binding to lymphocytes at pH 5.2 was also above 90%, but at pH 7.4 was 75% of total. At pH 5.2, both cell types displayed identical displacement curves of [125I]iodo-bTSH by unlabeled bTSH. Pure hCG, human placental lactogen, human GH, and insulin cross-reacted to less than 1% with [125I]iodo-bTSH binding to lymphocytes at pH 5.2, whereas a crude preparation of hCG and human FSH plus human LH showed a strong cross-reaction. Nonhormone glycoproteins, including mucin, normal human gamma-globulin, and bovine thyroglobulin showed intermediate cross-reactivity. At pH 7.4, the cross-reactivity of normal human gamma-globulin, bovine thyroglobulin, and pure hCG with bTSH binding to both lymphocytes and thyroid cells was below 1%. The TSH-binding properties of lymphocytes and thyroid cells show many similarities but differ in kinetics and the relative binding capacity at neutral pH. Although the physiological significance of these differences is not yet clear, cultured cells provide a convenient system for studies of TSH-receptor interaction.

L6 ANSWER 22 OF 34 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 1979147506 MEDLINE
DOCUMENT NUMBER: PubMed ID: 747894
TITLE: Thyroid hormone, oestrogen, and glucocorticoid effects on two different pituitary glycoprotein hormone alpha subunit pools.
AUTHOR: Kourides I A; Weintraub B D; Re R N; Ridgway E C; Maloof F
SOURCE: Clinical endocrinology, (1978 Dec) Vol. 9, No. 6, pp. 535-42.
Journal code: 0346653. ISSN: 0300-0664.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197906
ENTRY DATE: Entered STN: 15 Mar 1990
Last Updated on STN: 15 Mar 1990
Entered Medline: 11 Jun 1979

L6 ANSWER 23 OF 34 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1979:70553 BIOSIS
DOCUMENT NUMBER: PREV197917010553; BR17:10553
TITLE: COMPARATIVE UTILITY OF HUMAN PLACENTAL AND PITUITARY GLYCO PROTEIN HORMONES AND SUBUNITS AS TUMOR MARKERS.
AUTHOR(S): BLACKMAN M R; KOURIDES I A; ROSEN S W; WEINTRAUB B D
SOURCE: Clinical Research, (1978) Vol. 26, No. 3, pp. 303A.
CODEN: CLREAS. ISSN: 0009-9279.
DOCUMENT TYPE: Article
FILE SEGMENT: BR
LANGUAGE: Unavailable

L6 ANSWER 24 OF 34 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 1977118937 MEDLINE
DOCUMENT NUMBER: PubMed ID: 838863
TITLE: Metabolic clearance and secretion rates of subunits of

human thyrotropin.
AUTHOR: Kourides I A; Re R N; Weintraub B D; Ridgway E C; Maloof F
SOURCE: The Journal of clinical investigation, (1977 Mar) Vol. 59, No. 3, pp. 508-16.
Journal code: 7802877. ISSN: 0021-9738.
Report No.: NLM-PMC333388.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197704
ENTRY DATE: Entered STN: 13 Mar 1990
Last Updated on STN: 13 Mar 1990
Entered Medline: 25 Apr 1977

AB Metabolic clearance rates (MCR) of the alpha and beta subunits of human thyrotropin (hTSH-alpha and hTSH-beta) were determined by a constant infusion to equilibrium method. In 15 normal individuals (six men, six premenopausal women, and three post-menopausal women), the mean MCR of hTSH-alpha (68 ml/min per m2) was significantly faster than that of hTSH-beta (48 ml/min per m2) was significantly faster than that of hTSH-beta (48 ml/min per m2); both were two to three times more rapid than the previously determined MCR of hTSH. In patients with primary hypothyroidism, MCR were significantly slower with a mean value of 55 ml/min per m2 for hTSH-alpha and 37 ml/min per m2 for hTSH-beta. However, MCR of subunits were not significantly faster than normal in hyperthyroid patients. Serum concentrations of alpha subunits and hTSH-beta were measured by radioimmunoassay, and secretion rates of alpha and hTSH-beta from the pituitary were calculated using hTSH-alpha and hTSH-beta MCR, respectively. In the normal individuals, alpha secretion rates averaged 91 mug/day per m2, greater than those previously determined for hTSH and human follicle-stimulating hormone. Alpha
secretion rates were significantly elevated in the normal postmenopausal women (211 mug/day per m2) and in the premenopausal hypothyroid women (202 mug/day per m2); they were also elevated in the postmenopausal hypothyroid women (277 mug/day per m2). Alpha secretion rates were significantly decreased in the premenopausal hyperthyroid women (66 mug/day per m2). Usually, the secretion rates of hTSH-beta could not be calculated in normal individuals, and the rates in hyperthyroid patients could never be calculated because serum hTSH-beta was not detected. Six normals had detectable hTSH-beta secretion rates (17 mug/day per m2); hTSH-beta secretion rates were significantly increased in patients with primary hypothyroidism (28 mug/day per m2). Although we had previously demonstrated a 50-fold increase in hTSH secretion rates in primary hypothyroidism, there was only a 2-fold increase in alpha and hTSH-beta secretion rates. Thus, increased subunit synthesis appears to be utilized predominantly for production of complete hTSH.

L6 ANSWER 25 OF 34 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 1977184817 MEDLINE
DOCUMENT NUMBER: PubMed ID: 862556
TITLE: Combination of ectopic and standard human glycoprotein hormone alpha with beta subunits: discordance of immunologic and receptor-binding activity.
AUTHOR: Weintraub B D; Stannard B S; Rosen S W
SOURCE: Endocrinology, (1977 Jul) Vol. 101, No. 1, pp. 225-35.
Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197707
ENTRY DATE: Entered STN: 14 Mar 1990
Last Updated on STN: 14 Mar 1990
Entered Medline: 29 Jul 1977

L6 ANSWER 26 OF 34 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 1977223410 MEDLINE
DOCUMENT NUMBER: PubMed ID: 880552
TITLE: Placental proteins and their subunits as tumor markers in prostatic carcinoma.
AUTHOR: Broder L E; Weintraub B D; Rosen S W; Cohen M H; Tejada F
SOURCE: Cancer, (1977 Jul) Vol. 40, No. 1, pp. 211-6.
Journal code: 0374236. ISSN: 0008-543X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197709
ENTRY DATE: Entered STN: 14 Mar 1990
Last Updated on STN: 14 Mar 1990
Entered Medline: 17 Sep 1977
AB Sixteen patients with Stage D adenocarcinoma of the prostate were prospectively evaluated for the presence of human placental lactogen (hPL), placental alkaline phosphatase (PAP), and human chorionic gonadotropin (hCG). Ectopic production of hCG was found in one of the 16 cases and is described in detail. Serial serum hCG levels in that patient mirrored his course more reliably than concomitant acid phosphatase levels. Serum estradiol, testosterone, the hCG-alpha subunit, hPL and PAP were not elevated. There was a minimal elevation of serum FSH. There were no elevations of the other placental proteins in ten evaluable cases. A retrospective evaluation of serum bank specimens from 47 patients with prostatic carcinoma revealed no elevation of the placental proteins hPL, hCG-beta, and hCG-alpha. To our knowledge this report documents the first case of a chorionic gonadotropin-producing prostatic carcinoma appearing the literature.

L6 ANSWER 27 OF 34 MEDLINE on STN DUPLICATE 17
ACCESSION NUMBER: 1976174440 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1264211
TITLE: HeLa cells secrete alpha subunit of glycoprotein tropic hormones.
AUTHOR: Lieblich J M; Weintraub B D; Rosen S W; Chou J Y; Robinson J C
SOURCE: Nature, (1976 Apr 8) Vol. 260, No. 5551, pp. 530-2.
Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197607
ENTRY DATE: Entered STN: 13 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 6 Jul 1976

L6 ANSWER 28 OF 34 MEDLINE on STN
ACCESSION NUMBER: 1976237783 MEDLINE
DOCUMENT NUMBER: PubMed ID: 820707
TITLE: Secretion of alpha subunit of glycoprotein hormones by pituitary adenomas.

AUTHOR: Kourides I A; Weintraub B D; Rosen S W; Ridgway E C; Kliman B; Maloof F
SOURCE: The Journal of clinical endocrinology and metabolism, (1976 Jul) Vol. 43, No. 1, pp. 97-106.
Journal code: 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197610
ENTRY DATE: Entered STN: 13 Mar 1990
Last Updated on STN: 13 Mar 1990
Entered Medline: 1 Oct 1976

AB In 60 patients with pituitary adenomas, the serum concentration of the alpha subunit of the glycoprotein hormones (serum alpha) was measured by a sensitive and specific radioimmunoassay. Five patients had markedly elevated serum alpha prior to therapy (range 14.5-23.0 ng/ml). These 5 patients included 2 hyperthyroid men with inappropriately high serum thyrotropin, one of whom also had acromegaly, a man with hyperprolactinemia and elevated cerebrospinal fluid alpha, a postmenopausal woman with low serum gonadotropins and hyperprolactinemia, and a man with central hypothyroidism and hypogonadism. Three of the 5 were restudied after therapy; serum alpha in these three decreased from19.5 to 10.6, 23.0 to 2.0, and 17.0 to 12.0 ng/ml. Alpha in these 3 patinets' serum eluted similarly to normal pituitary alpha by gel chromatography. The other 55 patinets, including twenty with acromegaly, fifteen with galactorrhea, and two with Nelson's syndrome, had serum alpha.less than 0.5-5.0 ng/ml. In addition, 22 patients with "empty sella" syndrome (no pituitary tumor) had alpha less than 0.5-5.0 ng/ml. Normal men and premenopausal women had serum alpha concentrations of less than 0.5-2.5 ng/ml; normal postmenopausal women, 1.0-7.0 ng/ml; and patients with primary hypothyroidism, 0.7-9.0 ng/ml. The decreased alpha response to thyrotropin and luteinizing hormone-releasing hormones (TRH and LHRH) implied a relative autonomy of pituitary tumor alpha secretion; the mean alpha increment in the 5 patients with elevated serum alpha was 15% after TRH administration and 10% after LHRH. Normal individuals and patients with primary hypothyroidism demonstrated greater mean per cent alpha increments after TRH or LHRH. In certain patients with an enlarged sella turcica, an elevated serum alpha with little or no increase in secretion after TRH and LHRH may suggest the presence of pituitary tumor.

L6 ANSWER 29 OF 34 MEDLINE on STN DUPLICATE 18
ACCESSION NUMBER: 1976006077 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1159086
TITLE: Differences between purified ectopic and normal alpha subnits of human glycoprotein hormones.
AUTHOR: Weintraub B D; Krauth G; Rosen S W; Babson A S
SOURCE: The Journal of clinical investigation, (1975 Oct) Vol. 56, No. 4, pp. 1043-52.
Journal code: 7802877. ISSN: 0021-9738.
Report No.: NLM-PMC301960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197511
ENTRY DATE: Entered STN: 13 Mar 1990
Last Updated on STN: 13 Mar 1990
Entered Medline: 22 Nov 1975

AB "Ectopic" proteins, not distinguished immunologically from the common alpha subunit of the human glycoprotein hormones, were purified

approximately 10,000-fold from a gastric carcinoid tumor (A.L.-alpha) and from tissue culture medium of bronchogenic carcinoma cell lines (ChaGo-alpha). The purified A.L.-alpha was homogeneous by sodium dodecyl sulfate (SDS) gel electrophoresis while the purified ChaGo-alpha showed multiple components, some of which represented aggregated species. In SDS gel electrophoresis, the apparent molecular weights of A.L.-alpha (15,000) and dithioerythritol-reduced ChaGo-alpha (13,000) were significantly lower than those of the alpha subunits of human chorionic gonadotropin (hCG-alpha), luteinizing hormone, follicle-stimulating hormone, or thyroid-stimulating hormone (22,000-23,000). Binding experiments with [35S]-SDS suggested that these apparent differences in molecular weight resulted, at least in part, from diminished binding of the SDS by the normal compared to the ectopic alpha subunits. In gel chromatography, the apparent molecular weights of A.L.-alpha (27,000) and ChaGo-alpha (30,000) were slightly higher than those of normal alpha subunits (23,000-24,000). Both A.L.-alpha and ChaGo-alpha were not distinguished from hCG-alpha in ion-exchange chromatography. The composition of A.L.-alpha was similar to that of hCG-alpha in 13 amino acids but showed decreased phenylalanine and increased valine; glucosamine was identified in both A.L.-alpha and hCG-alpha. Under conditions in which hCG-alpha combined with the hCG beta subunit (hCG-beta) to produce 95% of the expected gonadotropin-binding activity in a rat testis radioreceptor-assay, A.L.-alpha incubation with hCG-beta resulted in only 2% of the expected activity, and ChaGo-alpha incubation with hCG-beta produced no detectable activity. These characteristics of ectopic alpha subunits may reflect abnormalities of neoplastic protein synthesis or carbohydrate attachment which result in polypeptides with chemical and immunologic similarity to normal subunits but with differences in physical and combining properties; alternatively, the ectopic subunits may represent as yet unrecognized alpha precursor forms.

L6 ANSWER 30 OF 34 MEDLINE on STN
ACCESSION NUMBER: 1975151912 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1127093
TITLE: Pituitary secretion of free alpha and beta subunit of human thyrotropin in patients with thyroid disorders.
AUTHOR: Kourides I A; Weintraub B D; Ridgway E C; Maloof F
SOURCE: The Journal of clinical endocrinology and metabolism, (1975 May) Vol. 40, No. 5, pp. 872-85.
Journal code: 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197507
ENTRY DATE: Entered STN: 10 Mar 1990
Last Updated on STN: 10 Mar 1990
Entered Medline: 23 Jul 1975
AB Utilizing sensitive and specific radioimmunoassays, serum concentrations of human thyrotropin (hTSH), the immunologically common alpha subunit of the glycoprotein hormones, and the specific beta subunit of hTSH (hTSH-beta) have been measured in normal individuals, in patients with primary hypothyroidism, and in patients with other disorders of thyroid function before and after intravenous administration of thyrotropin releasing hormone (TRH). In 29 normal individuals hTSH-beta was not detectable in serum (smaller than 0.5 ng/ml) before or after TRH; alpha was smaller than 0.5-2.0 ng/ml in men and premenopausal women and 1.0-5.0 ng/ml in postmenopausal women and did not increase after TRH. In 20 patients with primary hypothyroidism mean serum hTSH-beta was 1.3 ng/ml and increased to a peak value of 3.7 ng/ml after TRH; mean alpha was 4.3

ng/ml and increased to 6.3 ng/ml after TRH. None of the patients with Graves' disease, a hyperfunctioning thyroid nodule, or hypothyrotropic hypothyroidism had detectable serum hTSH-beta concentrations or alpha concentrations higher than the normals before or after TRH. In 3 patients with primary hypothyroidism given an intravenous bolus of labeled hTSH, no dissociation of hTSH into subunits was detectable for at least 3 h, indicating that the increment in serum alpha and hTSH-beta after TRH represented secretion of free subunits from the pituitary. In addition, L-thyroxine (L-T4) administered to 2 hypothyroid patients decreased the serum concentrations of alpha and hTSH-beta before and after TRH. Serum hTSH-beta was fully suppressed with 100-300 mug L-T4 daily, but there was a residual serum alpha component, which could not be suppressed with thyroid hormone and probably represented alpha subunits arising from gonadotropin-secreting pituitary cells. Normal pituitary glands also contained a predominance of free alpha subunit relative to hTSH-beta, in addition to hTSH. The secretion of free subunits in hypothyroidism may represent only a quantitative difference from the normal state, and subunits of hTSH appear to respond to the same control mechanisms as complete hTSH.

L6 ANSWER 31 OF 34 MEDLINE on STN DUPLICATE 19
ACCESSION NUMBER: 1974266599 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4135037
TITLE: Homologous radioimmunoassay of thyrotrophin in rat plasma.
AUTHOR: Kieffer J D; Weintraub B D; Baigelman W; Leeman S; Maloof F
SOURCE: Acta endocrinologica, (1974 Jul) Vol. 76, No. 3, pp. 495-505.
Journal code: 0370312. ISSN: 0001-5598.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197408
ENTRY DATE: Entered STN: 10 Mar 1990
Last Updated on STN: 10 Mar 1990
Entered Medline: 23 Aug 1974

L6 ANSWER 32 OF 34 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1975:59122 BIOSIS
DOCUMENT NUMBER: PREV197511059122; BR11:59122
TITLE: CHORIONIC GONADOTROPIN BINDING TO THE FOLLICLE STIMULATING HORMONE RECEPTOR OF RAT TESTIS.
AUTHOR(S): RABINOWITZ D; SCHWARTZ S; WEINTRAUB B D; ROTH J
SOURCE: Endocrinology, (1974) Vol. 94, No. SUPPL, pp. A-106.
CODEN: ENDOAO. ISSN: 0013-7227.
DOCUMENT TYPE: Article
FILE SEGMENT: BR
LANGUAGE: Unavailable

L6 ANSWER 33 OF 34 MEDLINE on STN DUPLICATE 20
ACCESSION NUMBER: 1971101807 MEDLINE
DOCUMENT NUMBER: PubMed ID: 5099999
TITLE: Monotropic increase of serum FSH correlated with low sperm count in young men with idiopathic oligospermia and aspermia.
AUTHOR: Rosen S W; Weintraub B D
SOURCE: The Journal of clinical endocrinology and metabolism, (1971 Mar) Vol. 32, No. 3, pp. 410-6.
Journal code: 0375362. ISSN: 0021-972X.

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PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:        197103
ENTRY DATE:         Entered STN: 1 Jan 1990
                    Last Updated on STN: 1 Jan 1990
                    Entered Medline: 23 Mar 1971

L6   ANSWER 34 OF 34     MEDLINE on STN                 DUPLICATE 21
ACCESSION NUMBER:   1970158285     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 5438302
TITLE:              Concentration and purification of human chorionic
                    somato-mammotropin (HCS) by affinity chromatography:
                    application to radioimmunoassay.
AUTHOR:             Weintraub B D
SOURCE:             Biochemical and biophysical research communications, (1970
                    Apr 8) Vol. 39, No. 1, pp. 83-9.
                    Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        197005
ENTRY DATE:         Entered STN: 1 Jan 1990
                    Last Updated on STN: 1 Jan 1990
                    Entered Medline: 26 May 1970


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     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:07:18 ON 10 DEC 2009
L1           227 SEA FILE=MFE SPE=ON  ABB=ON  PLU=ON  SZKUDLINSKI M?/AU
L2            22 SEA FILE=MFE SPE=ON  ABB=ON  PLU=ON  L1 AND (FSH OR FOLLICLE(W)
                   STIMULATING(W) HORMONE)
L3            10 DUP REM L2 (12 DUPLICATES REMOVED)
L4          1178 SEA FILE=MFE SPE=ON  ABB=ON  PLU=ON  WEINTRAUB B?/AU
L5            84 SEA FILE=MFE SPE=ON  ABB=ON  PLU=ON  L4 AND (FSH OR FOLLICLE(W)
                   STIMULATING(W) HORMONE)
L6            34 DUP REM L5 (50 DUPLICATES REMOVED)
                 DIS IBIB ABS L3 1-10

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     FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 15:14:17 ON 10 DEC 2009
                DIS IBIB ABS L6 1-34

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